What is claimed is:

Sub C1

1. A substantially homogeneous crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.26, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14 and, 26.91.

Sub E1

2. The polymorph of claim 1, characterized by the X-ray powder diffraction pattern shown in Figure 3.

Sub C2

3. A crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.26, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14 and, 26.91, which is substantially free of the A polymorph.

Sub F1

4. The polymorph of claim 3, characterized by the X-ray powder diffraction pattern shown in Figure 3.

Sub B1

5. A composition comprising a substantially homogeneous crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.26, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14 and, 26.91.

6. The composition of claim 5, wherein the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately:

2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)
6.255	100.0	17.668	2.5	22.982	4.8	27.534	0.9	32.652	1.7
7.860	3.2	18.193	0.7	23.589	2.3	28.148	1.5	33.245	1.7
9.553	3.9	18.749	1.5	23.906	3.0	28.617	4.3	34.719	1.5
11.414	1.5	19.379	1.0	24.459	6.8	29.000	1.4	35.737	0.8
12.483	6.4	20.196	14.4	25.138	10.0	29.797	2.1	36.288	1.0
13.385	9.6	20.734	4.2	25.617	3.7	30.267	0.9	36.809	0.6
14.781	2.1	21.103	14.4	25.908	3.9	30.900	1.6	37.269	1.1
15.720	2.9	21.873	4.7	26.527	2.8	31.475	2.2	37.643	1.4
16.959	5.5	22.452	4.5	26.911	5.6	31.815	2.4	38.114	1.7

7. The composition of claim 5, wherein the N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride in the polymorph B form is characterized by the X-ray powder diffraction pattern shown in Figure 3.

8. A composition comprising a crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.26, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14 and, 26.91 in a weight % of the B polymorph relative to the A polymorph which is at least 70%.

9. The composition of claim 8, wherein the B polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine exhibits an X-ray powder diffraction pattern having characteristic peaks expressed

Sub C5

16. The method of claim 14, wherein the method of for the treatment of a cancer selected from non-small cell lung cancer (NSCLC), refractory ovarian cancer, head and neck cancer, colorectal cancer and renal cancer.

15 17. The method of claim 14, wherein the therapeutically effective amount is from about 0.001 to about 100 mg/kg/day.

Sub E1

16 12 18. The method of claim 14, wherein the therapeutically effective amount is from about 1 to about 35 mg/kg/day.

17 12 19. The method of claim 14, wherein the therapeutically effective amount is from about 1 to about 7000 mg/day.

18 17 20. The method of claim 19, wherein the therapeutically effective amount is from about 5 to about 2500 mg/day.

19 18 21. The method of claim 20, wherein the therapeutically effective amount is from about 5 to about 200 mg/day.

20 19 22. The method of claim 21, wherein the therapeutically effective amount is from about 25 to about 200 mg/day.

Sub B3

23. A method for the treatment of a hyperproliferative disorder in a mammal which comprises administering to said mammal a therapeutically effective amount of the polymorph of claim 1 in combination with an anti-tumor agent selected from the group consisting of a mitotic inhibitor, an alkylating agent, an anti-metabolite, an intercalating antibiotic, a growth factor inhibitor, a cell cycle inhibitor, an enzyme, a topoisomerase inhibitor, a biological response modifier, an anti-hormone, and an anti-androgen.

in degrees 2-theta at approximately:

2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)
6.255	100.0	17.668	2.5	22.982	4.8	27.534	0.9	32.652	1.7
7.860	3.2	18.193	0.7	23.589	2.3	28.148	1.5	33.245	1.7
9.553	3.9	18.749	1.5	23.906	3.0	28.617	4.3	34.719	1.5
11.414	1.5	19.379	1.0	24.459	6.8	29.000	1.4	35.737	0.8
12.483	6.4	20.196	14.4	25.138	10.0	29.797	2.1	36.288	1.0
13.385	9.6	20.734	4.2	25.617	3.7	30.267	0.9	36.809	0.6
14.781	2.1	21.103	14.4	25.908	3.9	30.900	1.6	37.269	1.1
15.720	2.9	21.873	4.7	26.527	2.8	31.475	2.2	37.643	1.4
16.959	5.5	22.452	4.5	26.911	5.6	31.815	2.4	38.114	1.7

10. The composition of claim 8, wherein the N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride in the polymorph B form is characterized by the X-ray powder diffraction pattern shown in Figure 3.

11. A pharmaceutical composition which comprises a therapeutically effective amount of the polymorph of claim 1 and a pharmaceutically acceptable carrier.

12. The pharmaceutical composition of claim 11, wherein said composition is adapted for oral administration.

13. The pharmaceutical composition of claim 12, wherein the pharmaceutical composition is in the form of a tablet.

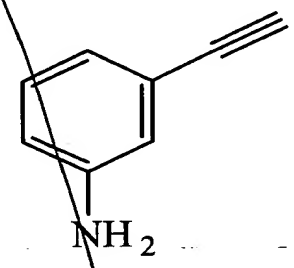
14. A method of treating a hyperproliferative disorder in a mammal which comprises administering to said mammal a therapeutically effective amount of the polymorph of claim 1.

15. The method of claim 14, wherein the method is for the treatment of a cancer selected from brain, squamous cell, bladder, gastric, pancreatic, breast, head, neck, oesophageal, prostate, colorectal, lung, renal, kidney, ovarian, gynecological and thyroid cancer.

24. A method of preparing a crystalline polymorph of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride designated the B polymorph which comprises the step of recrystallizing N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride in a solvent comprising alcohol.

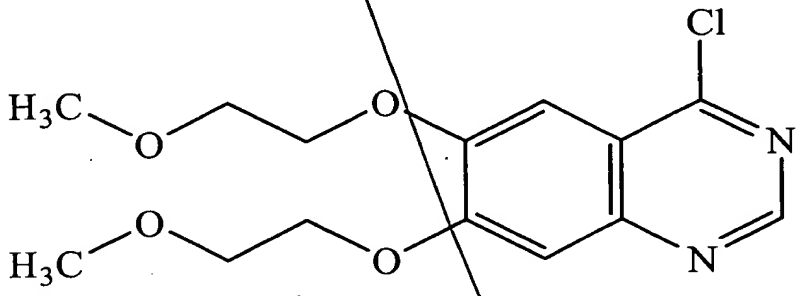
25. The method of claim 24, wherein the solvent further comprises water.

26. The method of claim 24, wherein N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride is prepared by coupling a compound of formula 6



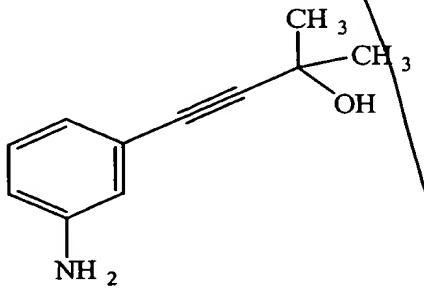
6

with a compound of formula 4



4.

27. The method of claim 26, wherein said compound of formula 6 is prepared by reacting a compound of formula 5



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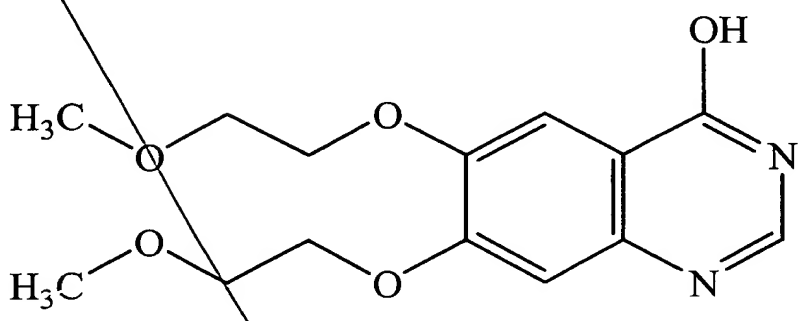
in a suspension of metal alkali and solvent and with heating.

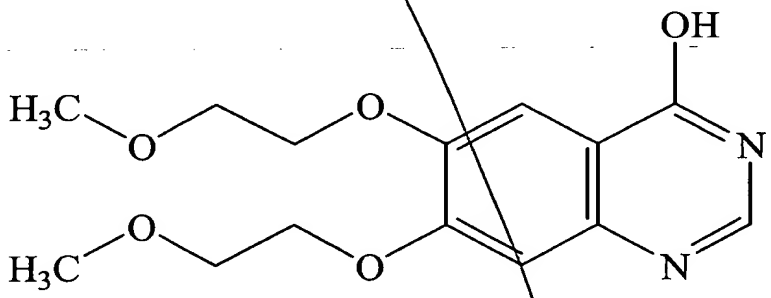
28. The method of claim 26, wherein said compound of formula 4 is prepared by chlorinating a compound of formula 3



3.

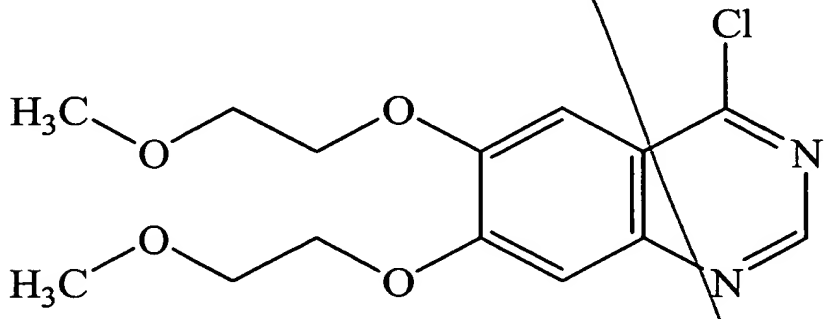
29. A method for the production of the polymorph B of claim 1 comprising the steps of:

a) substitution chlorination of starting quinazolinamine compound of formula 3



3

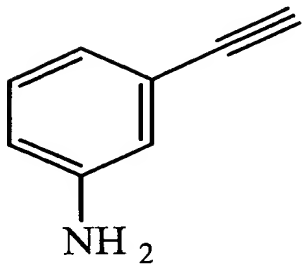
having an hydroxyl group, to provide a compound of formula 4



4

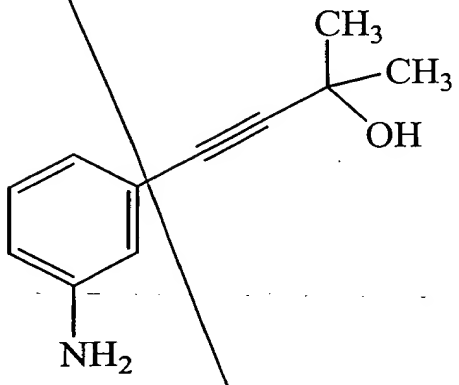
by reaction thereof in a solvent mixture of thionyl chloride, methylene chloride and dimethylformamide,

b) preparation of a compound of formula 6



6

Sub C7 in situ from starting material of compound of formula 5



5

by reaction of the latter in a suspension of metal alkali and solvent and with heating;

c) reaction of the compound of formula 6 in situ with the compound of formula 4 wherein the compound of formula 6 replaces the chlorine in the compound of formula 4 to give the N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride;

d) recrystallizing the N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride, in alcohol, into the polymorph B form.

30. The method of claim 29, wherein the substitution chlorination is quenched in the presence of aqueous sodium hydroxide.

31. The method of claim 29, wherein the substitution chlorination is quenched in the presence of aqueous sodium bicarbonate.

32. The method of claim 29, wherein the substitution chlorination is quenched in the presence of aqueous potassium hydroxide, aqueous potassium bicarbonate, aqueous potassium carbonate, aqueous sodium carbonate, or a mixture thereof.

33. A method for the production of a crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B polymorph by recrystallization comprising the steps of:

e) heating to reflux alcohol, water and the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine so as to form a solution;
f) cooling the solution to between about 65 and 70 °C;
g) clarifying the solution; and
h) precipitating polymorph B by further cooling the clarified solution.

34. A substantially homogeneous crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the A polymorph characterized by the X-ray powder diffraction pattern shown in Figure 1.

35. A crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the A polymorph characterized by the X-ray powder diffraction pattern shown in Figure 1, which is substantially free of the B polymorph.

36. A composition comprising a substantially homogeneous crystalline polymorph of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride designated the A polymorph, which is characterized by the following peaks in its X-ray powder diffraction pattern shown in Figure 1.

37. A composition comprising a substantially homogeneous crystalline polymorph of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride in the form of polymorph A, which is characterized by the following peaks:

Polymorph A

Anode: Cu- Wavelength 1: 1.54056 Wavelength 2:1.54439 (Rel Intensity: 0.500)

Range# 1 -Coupled: 3.000 to 40.000 StepSize: 0.040 StepTime: 1.00

Smoothing Width: 0.300 Threshold: 1.0

d(A)	I(rel)	d(A)	I(rel)	d(A)	I(rel)	d(A)	I(rel)	d(A)	I(rel)
15.82794	100.0	6.63179	1.7	4.54453	4.8	3.61674	8.2	2.91238	3.5
14.32371	3.9	5.84901	2.1	4.19685	4.7	3.50393	9.3	2.73148	3.7
11.74376	1.5	5.69971	2.3	4.16411	4.4	3.40200	6.0	2.60193	1.8
11.03408	1.2	5.46922	2.4	3.97273	4.7	3.35174	5.3	2.48243	1.3
10.16026	1.4	5.21396	3.6	3.91344	12.4	3.29005	4.2	2.40227	2.2
8.98039	13.1	4.80569	3.5	3.78223	24.2	3.05178	7.1	2.31297	1.7
7.85825	7.8	4.70077	12.2	3.67845	8.8	2.97750	3.0		

or,

Polymorph A

Anode: Cu - Wavelength 1: 1.54056 Wavelength 2: 1-54439 (Rel Intensity: 0.500)

Range#1 - Coupled: 3.000 to 40.000 StepSize: 0.040 StepTime: 1.00

Smoothing Width: 0.300 Threshold: 1.0

2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)
5.579	100.0	13.340	1.7	19.517	4.8	24.594	8.2	30.673	3.5
6.165	3.9	15.135	2.1	21.152	4.7	25.398	9.3	32.759	3.7
7.522	1.5	15.534	2.3	21.320	4.4	26.173	6.0	34.440	1.8
8.006	1.2	16.193	2.4	22.360	4.7	26.572	5.3	36.154	1.3
8.696	1.4	16.991	3.6	22.703	12.4	27.080	4.2	37.404	2.2
9.841	13.1	18.447	3.5	23.502	24.2	29.240	7.1	38.905	1.7
11.251	7.8	18.862	12.2	24.175	8.8	30.007	3.0		

38. A composition comprising a substantially homogeneous crystalline polymorph of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride in the form of polymorph B, which is characterized by the following peaks:

Polymorph B

Anode: Cu - Wavelength 1 1.54056 Wavelength 2: 1.54439 (Rel Intensity:0.500)

Range # 1 - Coupled 3.000 to. 40.040 StepSize: 0.040 StepTime 1.00

Smoothing Width: 0.300 Threshold: 1.0

d(A)	I(rel)	d(A)	I(rel)	d(A)	I(rel)	d(A)	I(rel)	d(A)	I(rel)
14.11826	100.0	5.01567	2.5	3.86656	4.8	3.23688	0.9	2.74020	1.7
11.23947	3.2	4.87215	0.7	3.76849	2.3	3.16755	1.5	2.69265	1.7
9.25019	3.9	4.72882	1.5	3.71927	3.0	3.11673	4.3	2.58169	1.5
7.74623	1.5	4.57666	1.0	3.63632	6.8	3.07644	1.4	2.51043	0.8
7.08519	6.4	4.39330	14.4	3.53967	10.0	2.99596	2.1	2.47356	1.0
6.60941	9.6	4.28038	4.2	3.47448	3.7	2.95049	0.9	2.43974	0.6
5.98828	2.1	4.20645	14.4	3.43610	3.9	2.89151	1.6	2.41068	1.1
5.63253	2.9	4.06007	4.7	3.35732	2.8	2.83992	2.2	2.38755	1.4
5.22369	5.5	3.95667	4.5	3.31029	5.6	2.81037	2.4	2.35914	1.7

or,

Polymorph B

Anode: Cu - Wavelength 1 1.54056 Wavelength 2: 1.54439 (Rel Intensity:0.500)

Range# 1 - Coupled: 3.000 to 40.040 StepSize 0.040 StepTime: 1.00

Smothing Width:0.300 Threshold: 1.0

2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)	2-Theta	I(rel)
6.255	100.0	17.668	2.5	22.982	4.8	27.534	0.9	32.652	1.7
7.860	3.2	18.193	0.7	23.589	2.3	28.148	1.5	33.245	1.7
9.553	3.9	18.749	1.5	23.906	3.0	28.617	4.3	34.719	1.5
11.414	1.5	19.379	1.0	24.459	6.8	29.000	1.4	35.737	0.8
12.483	6.4	20.196	14.4	25.138	10.0	29.797	2.1	36.288	1.0
13.385	9.6	20.734	4.2	25.617	3.7	30.267	0.9	36.809	0.6
14.781	2.1	21.103	14.4	25.908	3.9	30.900	1.6	37.269	1.1
15.720	2.9	21.873	4.7	26.527	2.8	31.475	2.2	37.643	1.4
16.959	5.5	22.452	4.5	26.911	5.6	31.815	2.4	38.114	1.7

39. A prodrug of the compound of claim 1.

40. A method of inducing differentiation of tumor cells in a tumor comprising contacting the cells with an effective amount of the compound of claim 1, or a composition of claims 3 or 6 so as to thereby differentiate the tumor cells.

41. A method for the treatment of NSCLC (non small cell lung cancer), pediatric malignancies, cervical and other tumors caused or promoted by human papilloma virus (HPV), melanoma, Barrett's esophagus (pre-malignant syndrome), adrenal and skin cancers and auto immune, neoplastic cutaneous diseases and atherosclerosis in a mammal comprising administering to said mammal a therapeutically effective amount of a pharmaceutical composition comprised of at least one of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine, and pharmaceutically acceptable salts thereof in anhydrous and hydrate forms.

42. The method of claim 41, wherein the treatment further comprises a palliative or neo-adjuvant/adjuvant monotherapy.

43. The method of claim 41, wherein the treatment further comprises blocking epidermal growth factor receptors (EGFR).

44. The method of claim 41, for use in treatment of tumors that express EGFRvIII.

45. The method of claim 41, wherein the treatment further comprises a combination with any of chemotherapy and immunotherapy

46. The method of claim 41, wherein the treatment further comprises, treatment with either or both anti-EGFR and anti-EGF antibodies.

47. The method of claim 41, wherein the treatment further comprises a further administration to said mammal of a member of the group consisting of inhibitors of MMP (matrix-metallo-proteinase), VEGFR (vascular endothelial growth factor receptor), farnesyl transferase, $CTLA_4$.(cytotoxic T-lymphocyte antigen 4) and erbB2, MAb to VEGFr, rhuMAb-VEGF, erbB2 MAb and avb3 Mab.

48. The method of claim 41, wherein the pharmaceutical compounds are used as radiation sensitizers for cancer treatment or in combination with anti-hormonal therapies.

49. The method of claim 41, wherein the pharmaceutical compounds are used for the inhibition of tumor growth in humans in a regimen with radiation treatment.

Sub B4

50. A method for the chemoprevention of basal or squamous cell carcinoma of the skin in areas exposed to the sun or in persons of high risk to said carcinoma, said method comprising administering to said persons a therapeutically effective amount of a pharmaceutical composition comprised of at least one of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine, and pharmaceutically acceptable salts thereof in anhydrous and hydrate forms.

51. A method of inducing differentiation of tumor cells in a tumor comprising contacting the cells with an effective amount of the compound of at least one of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine, and pharmaceutically acceptable salts thereof in anhydrous and hydrate forms.

Sub C9

52. A method of making a composition which composition comprises substantially homogeneous crystalline polymorph of the hydrochloride salt of N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine designated the B polymorph that exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2-theta at approximately 6.26, 12.48, 13.39, 16.96, 20.20, 21.10, 22.98, 24.46, 25.14 and, 26.91, comprising admixing the crystalline polymorph of claim 1 with a carrier.

53. The method of claim 52, wherein the N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride in the polymorph B form is characterized by the X-ray powder diffraction pattern shown in Figure 3.

Sub C9

54. The method of claim 52, wherein the carrier is a pharmaceutically acceptable carrier.

add B5

add C12

add E1